Formalities: AMENDMENT TO SPECIFICATION AND CLAIMS IN ACCORDANCE WITH 37 CFR 1.821-1.825

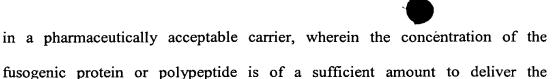
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As an initial matter, Applicant gratefully acknowledges the telephone conference with the Examiner on April 30, 2003, in which the proposed amendments to the claims and specification were discussed. Specifically, there is a problem with the current SEQ ID Nos. for the sequence listings in the present application. SEQ ID. Nos. 1 and 2 should represent fixed polypeptide sequences, while SEQ ID Nos. 3-6 should represent variable polypeptide sequences. However, in correcting an error with the reporting of these sequence listings (submission of November 4, 2002), SEQ ID Nos. 1 and 2 were inadvertently omitted and only SEQ ID Nos. 3-6 were provided to the Patent Office, but these were listed as SEQ ID Nos. 1-4. The net effect of this error is that it cancelled out the original SEQ ID Nos. 1 and 2. This error has been corrected herein in a re-submission of all sequence listings in this application which now read as SEQ ID Nos. 1-6.

Please amend claims 11, 25, 37 and 42 as follows:

- (Original) A method for delivering a pharmaceutical agent through a membrane, wherein the method comprises applying to said membrane a composition comprising:
 - a) anionic phospholipids;
 - b) a safe and effective amount of the pharmaceutical agent contained within the phospholipids; and
 - c) a fusogenic protein or polypeptide derived from prosaposin

polypeptide.



2) (Original) The method of claim 2 wherein the concentration of phospholipids are in at least a 10-fold excess, by weight, to that of the fusogenic protein or

pharmaceutical agent through the membrane.

- 3) (Original) The method of claim 2 wherein the pH of the composition is between about 5.5 and 2.
- 4) (Original) The method of claim 3 wherein the anionic phospholipid is an anionic liposome.
- 5) (Original) The method of claim 4 wherein the fusogenic protein or polypeptide is associated with the liposome through an electrostatic and hydrophobic interaction.
- 6) (Original) The method of claim 5 wherein the membrane is selected from the group consisting of dermal and mucosal membranes.
- 7) (Original) The method of claim 6 wherein the fusogenic protein or polypeptide is selected from the group consisting of saposin A, saposin C, polypeptide analogs, derivatives, homologues, fragments of saposin A and saposin C, and mixtures thereof.

- 8) (Original) The method of claim 6 wherein the fusogenic protein or polypeptide is saposin C.
- 9) (Original) The method of claim 6 wherein the fusogenic protein or polypeptide is SEQ. ID. NO. 1.
- 10) (Original) The method of claim 6 wherein the fusogenic protein or polypeptide is SEQ. ID. NO. 2.

11. (Currently Amended) The method of claim 6 wherein the fusogenic protein or polypeptide is of the formula given by SEQ ID Nos. 3-6.

h-u-Cys-Glu h Cys Glu h h h Lys Glu h-u-Lys h-h-Asp-Asn-Asn-Lys u Glu Lys Glu h h Asp h h Asp Lys h Cys u Lys h h,

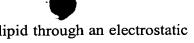
- where h hydrophobic amino acids, including, Val, Leu, Ile, Met, Pro, Phe, and Ala; and
- -u uncharged polar amino acids, including, Thr, Ser, Tyr, Gly, Gln, and Asn.
- 12) (Original) The method of claim 7 wherein administration of the composition is via a transdermal patch.
- 13) (Original) The method of claim 7 wherein the composition is administered either enterally or topically.

- 14) (Original) A method for delivering a pharmaceutical agent through either a dermal or mucosal membrane, wherein the method comprises the administration to said membrane of a composition comprising:
 - a) anionic liposomes;
 - b) a safe and effective amount of the pharmaceutical agent contained within the liposomes; and
 - c) saposin C;

in a pharmaceutically acceptable carrier, wherein the concentration of the liposomes are of a sufficient amount to deliver a safe and effective amount of the pharmaceutical agent through the membrane, the pH of the composition is between about 5.5 and 2, and the saposin C is associated with the surface of the liposome through an electrostatic and hydrophobic interaction.

- 15) (Original) The method of claim 14 wherein the concentration of the liposomes is in at least a 10-fold excess, by weight, to that of saposin C.
- 16) (Original) A therapeutic phospholipid composition comprising:
 - a) an anionic phospholipid;
 - b) a safe and effective amount of the pharmaceutical agent contained within the phospholipids; and
 - c) a fusogenic protein or polypeptide derived from prosaposin;

in a pharmaceutically acceptable carrier, wherein the concentration of the fusogenic protein or polypeptide is present in a sufficient concentration to deliver the pharmaceutical agent through a biological membrane and the fusogenic



protein or polypeptide is associated with the phospholipid through an electrostatic and hydrophobic interaction.

- 17) (Original) The phospholipid composition of claim 16 wherein the concentration of phospholipids is in at least a 10-fold excess, by weight, to that of the fusogenic protein or polypeptide.
- 18) (Original) The phospholipid composition of claim 17 wherein the pH of the composition is between about 5.5 and 2.
- 19) (Original) The phospholipid composition of claim 18 wherein the anionic phospholipid is an anionic liposome.
- 20) (Original) The phospholipid composition of claim 19 wherein the biological membrane is selected from the group consisting of dermal and mucosal membranes.
- 21) (Original) The phospholipid composition of claim 20 wherein the fusogenic protein or polypeptide is selected from the group consisting of saposin A, saposin C, polypeptide analogs, derivatives, homologues, fragments of saposin A and saposin C, and mixtures thereof.
- 22) (Original) The phospholipid composition of claim 20 wherein the fusogenic protein or polypeptide is saposin C.

- 23) (Original) The phospholipid composition of claim 20 wherein the fusogenic protein or polypeptide is SEQ. ID. NO. 1.
- 24) (Original) The phospholipid composition of claim 20 wherein the fusogenic protein or polypeptide is SEQ. ID. NO. 2.

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25) (Currently Amended) The phospholipid composition of claim 20 wherein the fusogenic protein or polypeptide is of the formula given by SEQ ID Nos. 3-6

h h u Cys Glu h Cys Glu h h Lys Glu h u Lys h h Asp Asn Asn Lys u Glu Lys Glu h h Asp h h Asp Lys h Cys u Lys h h,

-where h = hydrophobic amino acids, including, Val, Leu, Ile, Met, Pro, Phe, and Ala; and

-u - uncharged polar amino acids, including, Thr, Ser, Tyr, Gly, Gln, and Asn.

- 26) (Original) The phospholipid composition of claim 21 wherein the composition is formulated as part of a transdermal patch.
- 27) (Original) The phospholipid composition of claim 21 wherein the composition is formulated for enteral or topical administration.
- 28) (Original) A therapeutic phospholipid composition used to deliver a pharmaceutical agent through either a dermal or mucosal membrane, wherein the composition comprises:
 - a) anionic liposomes;

- b) a safe and effective amount of the pharmaceutical agent contained within the liposomes; and
- c) a fusogenic protein or polypeptide selected from the group consisting of saposin C, polypeptide analogs, derivatives, homologues, fragments of saposin C, and mixtures thereof;

in a pharmaceutically acceptable carrier where the pH of the composition is between about 5.5 and 2, wherein the concentration of the fusogenic protein or polypeptide is of a sufficient amount to deliver the pharmaceutical agent through a biological membrane and the fusogenic protein or polypeptide is associated with the surface of the liposome through an electrostatic and hydrophobic interaction.

- 29) (Original) The phospholipid composition of claim 28 wherein the concentration of the liposomes is in at least a 10-fold excess, by weight, to that of saposin C.
- 30) (Original) A composition comprising a safe and effective amount of a pharmaceutical agent contained in an anionic liposome, which is associated with a prosaposin-derived fusogenic protein or polypeptide via an electrostatic and hydrophobic interaction, wherein the concentration of the fusogenic protein or polypeptide is of a sufficient amount to deliver the pharmaceutical agent through a biological membrane, the composition contained in a pharmaceutically acceptable carrier, wherein the pH of the composition is between about 5.5 and 2.
- 31) (Original) The composition of claim 30 wherein the concentration of liposomes is in at least a 10-fold excess, by weight, to that of the fusogenic protein or polypeptide.

- 32) (Original) The composition of claim 31 wherein the biological membrane is selected from the group consisting of dermal and mucosal membranes.
- 33) (Original) The composition of claim 32 wherein the fusogenic protein or polypeptide is selected from the group consisting of saposin A, saposin C, polypeptide analogs, derivatives, homologues, fragments of saposin A and saposin C, and mixtures thereof.
- 34) (Original) The phospholipid composition of claim 31 wherein the fusogenic protein or polypeptide is saposin C.
- 35) (Original) The composition of claim 31 wherein the fusogenic protein or polypeptide is SEQ.ID.NO. 1.
- 36) (Original) The composition of claim 31 wherein the fusogenic protein or polypeptide is SEQ.ID.NO. 2.

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37. (Currently Amended) The composition of claim 31 wherein the fusogenic protein or polypeptide is of the formula given by SEQ ID Nos. 3-6.

h u Cys Glu h Cys Glu h h Lys Glu h u Lys h h Asp Asn Asn Lys u Glu Lys Glu h h Asp h h Asp Lys h Cys u Lys h h,

where h = hydrophobic amino acids, including, Val, Leu, Ile, Met, Pro, Phe, and Ala; and

u - uncharged polar amino acids, including, Thr, Ser, Tyr, Gly, Gln, and Asn.

- 38) (Original) A phospholipid composition used to deliver a pharmaceutical agent through either a dermal or mucosal membrane, wherein the composition comprises:
 - a) anionic liposomes;
 - b) a safe and effective amount of the pharmaceutical agent contained within the liposomes; and
 - c) saposin C;

in a pharmaceutically acceptable carrier, wherein the pH of the composition is between about 5.5 and 2, the concentration of the saposin C is of a sufficient amount to deliver the pharmaceutical agent through the membrane and the saposin C is associated with the surface of the liposome through an electrostatic and hydrophobic interaction.

- 39) (Original) The phospholipid composition of claim 38 wherein the concentration of the liposome is in at least a 10-fold excess, by weight, to that of saposin C.
- 40) (Original) The polypeptide of SEQ. ID. NO. 1.
- 41) (Original) The polypeptide of SEQ. ID. NO. 2.



42. (Currently Amended) A compound of the formula given by SEQ ID Nos. 3-6.

h u Cys Glu h Cys Glu h h h Lys Glu h u Lys h h Asp Asn Asn Lys u Glu Lys Glu h h Asp h h Asp Lys h Cys u Lys h h,

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where h = hydrophobic amino acids, including, Val, Leu, Ile, Met, Pro, Phe,

and Ala; and

u = uncharged polar amino acids, including, Thr, Ser, Tyr, Gly, Gln, and Asn.

- 43) (Original) A method for treating Gauchers Disease wherein the method comprises the administration of a composition comprising:
 - a) anionic liposomes;
 - b) a safe and effective amount of acid beta-glucosidase contained within the liposomes; and
 - c) saposin C;

in a pharmaceutically acceptable carrier, wherein the pH of the composition between about 5.5 and 2, the concentration of the saposin C is of a sufficient amount to deliver the pharmaceutical agent through the membrane and the saposin C is associated with the surface of the liposome through an electrostatic and hydrophobic interaction.

44) (Original) The method of claim 43 wherein the concentration of the liposome is in at least a 10-fold excess, by weight, to that of saposin C.